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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,857	01/30/2006	Melwyn Abreo	17243002001	2274

22511 7590 05/21/2008
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EXAMINER

JARRELL, NOBLE E

ART UNIT	PAPER NUMBER
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1624

NOTIFICATION DATE	DELIVERY MODE
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05/21/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/566,857	Applicant(s) ABREO ET AL.	
	Examiner Noble Jarrell	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 and 53-71 is/are pending in the application.
- 4a) Of the above claim(s) 26-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 and 53-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/30/06;11/09/07;3/28/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II in the reply filed on 3/28/2008 is acknowledged. The traversal is on the ground(s) that all of the groups share a common core. This is not found persuasive because the pyridine-piperazine portion of the different formulae only defines a third of the entire molecule due to the presence of variables W, V, R², and R³.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 60/491080 and 60/491322, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. These provisional applications fail to provide any support for the elected group.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-25 and 53-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a stereoisomer, enantiomer, or tautomer of the different formulae of the elected group, does not reasonably provide enablement for any prodrug of any of the formulae. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicants do not prepare any prodrug of any of the formulae of the elected group, and are therefore not enabled for prodrugs.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) *The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds and/or compositions of formula I where one-third of the molecule has pyridine-piperazine core. Thus, the claims taken together with the specification imply that these compounds are able to inhibit hSCD and in turn, treat or prevent a disorder caused by the enzyme.

(3) *The state of the prior art and (4) the predictability or unpredictability of the art:*

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Stella (*Expert Opinion in Therapeutic Patents*, **2004**, 14(3), 277-280) teaches that prodrug development has significant challenges to overcome and requires undue experimentation.

(5) The relative skill of those in the art:

One of ordinary skill in the art can replicate a procedure described in scheme 2 of the specification (page 46) to prepare a compound that falls within the elected group.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of a stereoisomer, enantiomer, or tautomer of the different formulae of the elected group.

However, the specification does not provide guidance for preparation of a prodrug of formulae of the elected group.

(8) The quantity of experimentation necessary:

Stella (*Expert Opinion in Therapeutic Patents*, **2004**, 14(3), 277-280) teaches that prodrug development has significant challenges to overcome and requires undue experimentation.

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-25 and 53-71 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 1-25 and 53-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In each of these claims, a compound and a pharmaceutical composition is being claimed. Because the scope of the claims is unclear, the claim is indefinite. In addition, these claims are unclear because of one possibility for variable R^2 , "a multi-ring structure having 2 to 4 rings" is indefinite. What rings are forming can be part of these systems? Applicants say that the rings can be cycloalkyl, heteroalkyl, aryl, or heteroaryl. Even with the definitions provided in the specification, these terms are still broad. The pyridine-piperazine portion of the molecule only defines a third of the various formulae, and a structure where variable R^2 includes a pyrazine ring would control classification of formula I then.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 10, 13, 14, 25, 53, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6677452, issued January 13, 2004, filed September 30, 1999). Chen et al. teach a compound of example 1 (columns 31-32) with a registry number of

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334002-42-5. In this compound, instant variables R^1 and R^2 are H and R^3 is phenyl.

Compositions of these compounds are taught from page 22, line 32 to page 23, line 17. This compound is considered a positional isomer of compound of the elected group. *In re Norris* (84 USPQ 458) teaches:

Novel and useful chemical compound, which is isomeric with compounds of prior art, is not patentable where new compound is not shown to possess new and unexpected utilities.

In re Wood (199 USPQ 137) teaches that H vs. Me is not considered a patentable advance evidence superior, unexpected result.

Thus, Chen et al. render compounds of the elected group obvious. Applicants are encouraged to look for other species within Chen et al. that may render compounds of the elected group obvious.

10. Claims 1-25, 53-58, 61, and 70-71 rejected under 35 U.S.C. 103(a) as being unpatentable over Fu et al. (US20050119251, published June 2, 2005, filed July 6, 2004, priority to 60/343516, filed December 21, 2001). Fu et al. teach examples 1-8 (pages 20-23). In examples 1-8, variable R^1 is H and R^2 is $(CH_2)_2$ -cyclopropyl, $(CH_2)_2$ -cyclobutyl, $(CH_2)_3$ -cyclopropyl, $(CH_3)_2CH(CH_2)_2$, and $(CH_3)_3C(CH_2)_2$. Variable R^3 is 2- CF_3 -phenyl or 5-fluoro-2- CF_3 -phenyl in each of the examples. Compositions comprising these examples are taught in paragraph 0186, pages 14-15. Fu et al. are using examples 1-8 and the rest of the prepared compounds for the same method of use as the instant invention. Each example is considered a positional isomer of compounds of the elected group. *In re Norris* (84 USPQ 458) teaches:

Novel and useful chemical compound, which is isomeric with compounds of prior art, is not patentable where new compound is not shown to possess new and unexpected utilities.

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Applicants are encouraged to look for any other species taught by Fu et al. that render compounds of the elected group obvious. Thus, compounds of the elected group are rendered obvious by Fu et al.

Double Patenting

11. Claim 71 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 57. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since the scope of claim 57 is currently unclear as to whether it is a compound or composition claim, claim 71 is considered a duplicate of claim 57.

12. Claim 24 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since the scope of claim 1 is currently unclear as to whether it is a compound or composition claim, claim 25 is considered a duplicate of claim 1.

13. Claim 56 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 53. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since the scope of claim 53 is currently unclear as to whether it is a compound or composition claim, claim 56 is considered a duplicate of claim 53.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting

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rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No.

11/815739. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound on page 37, line 18, of application 11/815739 can be embraced by the specified claims in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 1-10, 12-15, 18-19, and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 16-20, 22, 25, and 28 of copending Application No. 10/566193 (US PGPub 20060199802). Although the conflicting claims are not identical, they are not patentably distinct from each other because examples 3 to 3.9 of application 10/566193 can be embraced by the specified claims in both applications. Regarding claim 19 of 10/566857, the three compounds are rendered obvious by claim 22 of 10/566193 (specifically the second, first, and third compounds, respectively).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**